

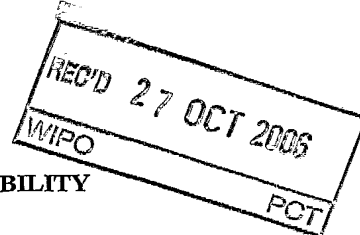
# PATENT COOPERATION TREATY

## PCT

### INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)



Applicant's or agent's file reference 014811-312.114WO	<b>FOR FURTHER ACTION</b>	See Form PCT/IPEA/416
International application No. PCT/US04/16784	International filing date (day/month/year) 27 May 2004 (27.05.2004)	Priority date (day/month/year) 24 June 2003 (24.06.2003)
International Patent Classification (IPC) or national classification and IPC IPC: CO7K 1/113, 14/535, 7/00; A61K 38/00 USPC: 530/, 307, 351, 313, 345; 514/2, 3, 8, 12, 13		
Applicant NOBEX CORPORATION		
1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36. 2. This REPORT consists of a total of <u>5</u> sheets, including this cover sheet. 3. This report is also accompanied by ANNEXES, comprising: a. <input type="checkbox"/> (sent to the applicant and to the International Bureau) a total of ___ sheets, as follows: <input type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions). <input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box. b. <input type="checkbox"/> (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) _____, containing a sequence listing and/or tables related thereto, in electronic form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).		
4. This report contains indications relating to the following items: <div style="display: flex; flex-direction: column; gap: 5px;"> <div><input checked="" type="checkbox"/> Box No. I      Basis of the report</div> <div><input type="checkbox"/> Box No. II      Priority</div> <div><input type="checkbox"/> Box No. III      Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</div> <div><input type="checkbox"/> Box No. IV      Lack of unity of invention</div> <div><input checked="" type="checkbox"/> Box No. V      Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability, citations and explanations supporting such statement</div> <div><input type="checkbox"/> Box No. VI      Certain documents cited</div> <div><input type="checkbox"/> Box No. VII      Certain defects in the international application</div> <div><input type="checkbox"/> Box No. VIII      Certain observations on the international application</div> </div>		
Date of submission of the demand 01 February 2005 (01.02.2005)	Date of completion of this report 04 October 2006 (04.10.2006)	
Name and mailing address of the IPEA/US Mail Stop PCT, Attn: IPEA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (571) 273-3201	Authorized officer  Samuel W. Liu Telephone No. 571-272-1600	

**Box No. I Basis of the report**

1. With regard to the **language**, this report is based on:

- ☐ the international application in the language in which it was filed.
- ☐ a translation of the international application into \_\_\_\_\_, which is the language of a translation furnished for the purposes of:
- ☐ international search (under Rules 12.3 and 23.1(b))
- ☐ publication of the international application (under Rule 12.4(a))
- ☐ international preliminary examination (under Rules 55.2(a) and/or 55.3(a))

2. With regard to the **elements** of the international application, this report is based on (*replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report*):

- ☒ the international application as originally filed/furnished
- ☒ the description:  
pages 1-104 as originally filed/furnished  
pages\* NONE received by this Authority on \_\_\_\_\_  
pages\* NONE received by this Authority on \_\_\_\_\_
- ☒ the claims:  
pages 105-109 as originally filed/furnished  
pages\* NONE as amended (together with any statement) under Article 19  
pages\* NONE received by this Authority on \_\_\_\_\_  
pages\* NONE received by this Authority on \_\_\_\_\_
- ☒ the drawings:  
pages 1-20 as originally filed/furnished  
pages\* NONE received by this Authority on \_\_\_\_\_  
pages\* NONE received by this Authority on \_\_\_\_\_
- ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:

- ☐ the description, pages \_\_\_\_\_
- ☐ the claims, Nos. \_\_\_\_\_
- ☐ the drawings, sheets/figs \_\_\_\_\_
- ☐ the sequence listing (*specify*): \_\_\_\_\_
- ☐ any table(s) related to the sequence listing (*specify*): \_\_\_\_\_

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

- ☐ the description, pages \_\_\_\_\_
- ☐ the claims, Nos. \_\_\_\_\_
- ☐ the drawings, sheets/figs \_\_\_\_\_
- ☐ the sequence listing (*specify*): \_\_\_\_\_
- ☐ any table(s) related to the sequence listing (*specify*): \_\_\_\_\_

*\* If item 4 applies, some or all of those sheets may be marked "superseded."*

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.  
PCT/US04/16784

**Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)

Claims 1-13 YES  
Claims NONE NO

Inventive Step (IS)

Claims NONE YES  
Claims 1-13 NO

Industrial Applicability (IA)

Claims 1-13 YES  
Claims NONE NO

2. Citations and Explanations (Rule 70.7)  
Please See Continuation Sheet

## Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Continuation of:

V. 2. Citations and Explanations:

Claims 1-13 lack inventive step under PCT Article 33(3) as being obvious over Ekwuribe et al. (US 2003/0060606), Camble et al. (US Pat. No. 5773581), Lee et al. (Pharm. Res, (1999) 16, 813-818) (A), Lee et al. (Pharm. Res. (2002) 19, 845-851) (B), and Lucke et al. (Biomaterials (2000) 21, 2361-2370).

In the patent claims 33-72, Ekwuribe et al. teach a method of treating a disease state, e.g., osteoporosis Paget's disease comprising administering to a subject a calcitonin conjugated with polyethylene glycol (PEG), wherein the PED moieties are linked to lysine residues 11 and 18 (see the patent claims 44). Since it is well-known fact that Paget's disease is a chronic bone disorder that typically results in enlarged, deformed bones and may result in bone pain (a peripheral pain), arthritis, the Ekwuribe's teaching is applied to claims 1-2. Also, Camble et al., Lee et al. (A), Lee et al. (B), and Lucke et al. teach the subject matter of the instant claims 1-2.

In the patent claims 45 and 50, Ekwuribe et al. teach that the PEG moiety consists of 7 PEG subunits (i.e., -[CH<sub>2</sub>CH<sub>2</sub>O]<sub>7</sub>-), which is covalently linked to a carboxylic acid moiety, as applied to claims 3-4.

In the patent claim 51, Ekwuribe et al. teach the same structure of claim 5, as applied to the instant claim 5.

In the patent claim 49, Ekwuribe et al. teach the same structure of claim 6, as applied to the instant claim 6.

## Supplemental Box

In the patent claims 46 and 51, Ekwuribe et al. teach the same structures of claims 7 and 8, respectively, as applied to the instant claims 7-8.

In the patent claims 52, 54, 55 and 56, Ekwuribe et al. teach the same structures of claims 9, 10, 11 and 12, as applied to the instant claims, 9, 10, 11 and 12.

In the patent claim 57, Ekwuribe et al. teach the same structure limitations as the formula A of the instant claim 13, which is applied to claim 13.

Ekwuribe et al. do not expressly teach the said method is applied to treating peripheral pain in said subject.

It would have been obvious to one skilled in the art at the time the invention was made to develop the method of treating peripheral pain comprising administering to said subject the PEG polymer or polyalkylene glycol conjugated calcitonin peptide. The one skilled in the art would have been motivated to do this because (i) calcitonin has been suggested for use in treating peripheral pain condition as taught by May et al.; and (ii) as stated above, the osteoporosis Paget's disease typically results in enlarged, deformed bones, i.e., arthritis pain - a peripheral pain condition; hence, treatment of osteoporosis Paget's disease by the Ekwuribe's PDE-conjugated calcitonin would have unavoidably led to treatment of the peripheral pain because the said pain is caused by the mentioned Paget's disease state. Thus, one skilled in the art would have readily and successfully arrived at the claimed process of the current application.

Claims 1-13 meet the requirement of PTC article 33(4), because the claimed process is useful for treating peripheral pain condition thereof.